REINHART | BOERNER | VAN DEUREN
NORRIS & RIESELBACH, S.C.

ATTORNEYS AT LAW

COPY

2227 '99 APR -5 P1:40

RECEIVED 99 MAR 29 PM 1:49

March 19, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Sir/Madam:

Re: Draft Federal/State Memorandum of Understanding on Interstate Distribution of Compounded Drug Products
Docket No. 98N-1265

On behalf of Madison Pharmacy Associates, Inc., a Wisconsin pharmacy that specializes in compounding, we are writing to provide comments to the Draft Federal/State Memorandum of Understanding on Interstate Distribution of Compounded Drug Products (the "Draft MOU").

Since 1982, Madison Pharmacy Associates has specialized in compounding hormonal drug products that are prescribed for high-risk pregnancies, premenstrual syndrome, and peri-menopause and menopause hormone replacement therapy. Madison Pharmacy Associates works with patients' physicians to determine the levels of estrogen, progesterone and other hormones in the compounded products based on testing performed on individual patients. Physicians from all over the country refer patients to this pharmacy so that Madison Pharmacy Associates can prepare their prescriptions according to the patient's individual hormone levels. A trained pharmacist compounds each drug product for an individual patient, pursuant to a physician's prescription, and provides counseling to the patient regarding the prescription, as is required under state pharmacy regulations.

The services that Madison Pharmacy Associates provides these patients and physicians are not available from commercial pharmaceutical manufacturers, nor from most local pharmacies. Many specialty pharmacies that compound a large portion of their prescriptions provide a singular service to patients with needs that

98N-1265 C811

22 East Mifflin Street Suite 600 P.O. Box 2020 Madison, Wisconsin 53701-2020 Telephone (608) 229-2200 Facsimile (608) 229-2100

Denver, CO (303) 831-0909 | Madison, WI (608) 229-2200 | Milwaukee, WI (414) 298-1000 | Washington, D.C. (202) 393-3636

03-29-1999 0023

cannot be met by drug products that are available from pharmaceutical manufacturers, e.g., nutritional formulations for AIDS patients with wasting syndrome; formulations of drugs without certain preservatives to which some patients are allergic; compounded drugs for pediatric patients, to alter doses or make the medication more palatable; and pain medications in suppository form for patients who cannot swallow medication. Compounding is also important in dermatology, intravenous solution therapies, oncology, and hospices. If the Draft MOU is finalized as written, these patients will be deprived of vital therapeutic options, unless they happen to live in a state with a pharmacy that specializes in compounding the particular drug that they need. Considering that the Draft MOU, if implemented, is likely to put many specialty compounding pharmacies out of business, even the option of finding a local pharmacy capable of compounding these medications will not be available to many of these patients. Such a result is not consistent with the protection of public health nor with the compounding provisions of the Food and Drug Administration Modernization and Accountability Act of 1997 ("FDAMA"), codified at 503A of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 353a.

Madison Pharmacy Associates opposes the Draft MOU on the following grounds:

I. The Draft MOU Impermissibly Deprives State Agencies Of Discretion In The Regulation Of Compounding To A Degree Not Contemplated By FDAMA.

By defining "inordinate amount" as a numeric cap on prescriptions distributed interstate and by mandating that state agencies take regulatory actions to enforce FDAMA, the Draft MOU deprives states of their discretion and authority to regulate pharmacy compounding in conflict with FDAMA.

The Draft MOU contains a definition of "inordinate amounts" that arbitrarily sets a percentage limit on the prescriptions that can be compounded and distributed interstate by a pharmacy. Arbitrarily limiting compounding to a percentage of each pharmacy's business is not consistent with the legislative

history of the FDAMA. According to the Report on FDAMA issued by the Senate Committee on Labor and Human Resources, "'[inordinate' quantities means amounts typically associated with ordinary commercial drug manufacturing." S. Rep. No. 105-43, at 68 (1997). The legislation requires that the MOU "address" the distribution of compounded drugs interstate. State pharmacy boards have been and continue to be quite capable of monitoring the compounding done by pharmacies and ensuring that the pharmacist-physician-patient triad remains intact. The MOU should address ways such monitoring should be done, and how FDA would become involved if a pharmacy was suspected of conducting commercial manufacturing under the guise of compounding. Instead, the Draft MOU makes no attempt to relate its definition of inordinate amounts to ordinary commercial drug manufacturing.

Defining "inordinate amounts" as a percentage limit is contrary to good pharmacy practice, since pharmacies that compound on a regular basis and which provide this service as a large portion of their business will generally have more knowledge, skill and experience with compounding than pharmacies that compound less frequently. There is nothing intrinsic to the process of compounding that results in these products becoming dangerous when sent across state lines, nor when a percentage of a particular pharmacy's prescriptions reach a certain number. As long as the prescriptions are compounded within the scope of pharmacy practice, i.e., each compounded prescription is prescribed by a physician and prepared by the pharmacist for an individual patient, then the amounts compounded will not become inordinate.

"Inordinate amounts" should be defined by the state pharmacy board based on the scope of pharmacy practice and the protection of patients. Pharmacists that specialize in compounding are best equipped to ensure protection of patients, because they have the training and expertise that makes quality assurance possible. Even one prescription compounded by a pharmacist who lacks this expertise could be considered "inordinate." Thus, even if a specialty pharmacy sends 95% of its compounded prescriptions out of state, such an amount would not be "inordinate" so long as trained pharmacists utilize extensive quality controls to ensure that the

prescriptions are compounded properly, and the other traditional requirements of compounding are met, i.e., the pharmacy is not actually manufacturing drugs.

Rather than respecting the discretion of state agencies to determine whether a pharmacy is engaging in manufacturing and how enforcement resources should be targeted, the Draft MOU dictates the actions that state agencies must take related to pharmacy compounding, Under the Draft MOU, the State agency "agrees to investigate complaints" and "will take regulatory action" regarding the distribution of compounded drugs interstate. Section III.B.4. and III.B.4.d. The decision whether to initiate an investigation of a particular pharmacy or pharmacist and how to enforce applicable pharmacy statutes has traditionally been and should remain within the discretion of the state agency. By signing the Draft MOU, a state agency would be relinquishing this discretion, a result not required by FDAMA nor contemplated by Congress.

In addition, the Draft MOU requires the state agency to "affirm[] that it now possesses and shall maintain, at the discretion of the State legislature, the legal authority (under State statutes and/or regulations) and the resources necessary to effectively carry out all aspects of this MOU." Section III.A. By this language, it appears that FDA is trying to mandate through the Draft MOU that state agencies devote state resources to FDA's enforcement duties--an approach that is not contemplated by the words of the statute, nor intended by Congress. In fact, in an analysis required by the Unfunded Mandates Reform Act, the Congressional Budget Office estimated that compliance with FDAMA would result in no significant costs for state and local governments. Yet FDA's Draft MOU not only acknowledges that the resources of state agencies will be needed to carry out the MOU, it requires that state agencies affirm that they possess and will maintain such resources.

II. Even If FDAMA Allows FDA To Define "Inordinate Amount" The Draft MOU's Definition Of "Inordinate Amount" Cannot Be Used As An Enforcement Standard Because It Has Not Been Promulgated Through Notice And Comment Rulemaking As Required Under The Administrative Procedures Act.

Even if FDA had the authority under FDAMA to define inordinate amounts instead of leaving such regulation to the states, it could only do so through notice-and-comment rulemaking. Under the Administrative Procedures Act ("APA"), 5 U.S.C. § 553, the definition of "inordinate amounts" is actually a legislative rule which cannot be issued through a memorandum of understanding. Under the APA, a "rule" is "the whole or a part of an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy . ..." 5 U.S.C. § 551(4). Under § 553 of the APA, agency rules may be issued only after the notice-and-comment procedures enumerated in the statute are completed.

The Draft MOU sets out the standard for "inordinate amount" as follows:

> "C. Distribution of Inordinate Amounts of Compounded Drugs
>
> 1. The [State agency] agrees to take action regarding any pharmacist, pharmacy, or physician within its jurisdiction who distributes inordinate amounts of compounded drugs interstate. Such action may include State regulatory action, referral to FDA for action, or joint State-FDA action. For the purposes of this MOU, interstate distribution of an inordinate amount of compounded drugs occurs under either of the following circumstances. . ." [emphasis added]. Draft MOU, Section III.C.1.

Under the APA's definition of rule stated above, this statement, and the Draft MOU's following two "circumstances" defining inordinate amounts, constitute a rule: it is an agency statement of "future effect designed to implement, interpret, or prescribe law or policy . ..."

In Community Nutrition Institute v. Young, 818 F.2d 943,945 (D.C. Cir. 1987), the D.C. Circuit Court of Appeals noted that there are two criteria that courts have used in determining whether a rule is legislative or interpretive. If a pronouncement (1) has a present, binding effect and (2) does not leave the agency and its decisionmakers free to exercise discretion, then it is a rule requiring notice-and-comment rulemaking. 818 F.2d at 946 (citation omitted). The Court of Appeals went onto state that courts should give far greater weight to the actual language used by the agency than to the agency's characterization of its statement, noting that it has "found decisive the choice between the words 'will' and 'may'" (citing *American Bus Association v. United States, 627* F.2d 525,532 (use of "will" indicates statement is in fact a binding norm) compared to *Guardian Federal Savings &Loan Ass 'n v. FSLIC 589* F.2d 658,666 (use of "may" indicates statement is a "general statement of policy'')). In applying this standard to a nonregulatory action level for aflatoxin at which com would be considered adulterated, the Court found significant the fact that FDA conceded that it would have difficulty prosecuting a producer for shipping corn with less than amount set forth as the action level. 818 F.2d at 948. The court held that FDA action levels setting the allowable level of aflatoxins in corn were invalid because they were substantive rules and FDA had failed to follow the notice-and-comment requirements. 818 F.2d at 949.

In applying this test to the language of the MOU, it is clear that the MOU is a rule, not a mere "statement of policy." As discussed above, by signing the MOU, a state agency is bound to take action. Several sections of the MOU use definitive language such as "will" rather than "may" in specifying how states will address complaints related to compounding pharmacies. See Draft MOU Sections III.B.2.; III.B.4.c and d; III.C. 1.; III.D. 1-3. For example, with respect to Section III.C. 1, quoted above, although the particular type of action the state must take is discretionary, the Draft MOU does not give states the option of taking no action against a pharmacy that dispenses the specified inordinate amount of compounded prescriptions. Therefore, at least the portion of the Draft MOU which defines

inordinate amount is a substantive rule that must meet the notice-and-comment requirements of 5 U.S.C. § 553.

Although FDA has the authority to enforce FDAMA without promulgating regulations, it would have difficulty prosecuting a pharmacy for distributing compounded products at levels below those specified in the Draft MOU, an indication under the reasoning in Community Nutrition that the MOU will contain a rule. Even prosecuting a pharmacy for distributing compounded products under the Draft MOU's definition of "inordinate amounts" would present problems for FDA, since the Draft MOU's definition cannot be legitimately relied on as a standard for enforcement and has no relation to the intent of Congress in passing FDAMA. The issuance of an MOU with the states prior to the promulgation of regulations under FDAMA thus results in a "Catch-22" for state agencies. The action that the MOU requires state agencies to take is an enforcement of federal law, but the standard for enforcement only exists in the MOU. Presumably, state agencies are expected to "take action" under their own jurisdiction. [1] In fact, state agencies already can take action against pharmacies that are believed to be engaging in manufacturing. Under the Draft MOU, however, state agencies would be enforcing a federal law, and would have to refer to the MOU for a definition of "inordinate amounts" in order to enforce a federal law that the FDA itself could not enforce.

A legally permissible approach would be for the MOU to instruct the state agency to determine what level of compounding would constitute inordinate amounts. The state agency could then make its own determination of the most appropriate level for compounding, under existing state pharmacy laws regulating manufacturing, compounding, and distributing of drug products. Such an approach would be consistent with the APA, FDAMA and the long-standing authority of state agencies to regulate the practice of pharmacy.

---

[1] In Wisconsin, the pharmacy statute defines "unprofessional conduct" to include violating any "federal .,. statute or rule which substantially relates to the practice of pharmacy." Wis. Stat. § 450.10(1)(a)2.

inordinate amount is a substantive rule that must meet the notice-and-comment requirements of 5 U.S.C. § 553.

Although FDA has the authority to enforce FDAMA without promulgating regulations, it would have difficulty prosecuting a pharmacy for distributing compounded products at levels below those specified in the Draft MOU, an indication under the reasoning in Community Nutrition that the MOU will contain a rule. Even prosecuting a pharmacy for distributing compounded products under the Draft MOU's definition of "inordinate amounts" would present problems for FDA, since the Draft MOU'S definition cannot be legitimately relied on as a standard for enforcement and has no relation to the intent of Congress in passing FDAMA. The issuance of an MOU with the states prior to the promulgation of regulations under FDAMA thus results in a "Catch-22" for state agencies. The action that the MOU requires state agencies to take is an enforcement of federal law, but the standard for enforcement only exists in the MOU. Presumably, state agencies are expected to "take action" under their own jurisdiction. [1] In fact, state agencies already can take action against pharmacies that are believed to be engaging in manufacturing. Under the Draft MOU, however, state agencies would be enforcing a federal law, and would have to refer to the MOU for a definition of "inordinate amounts" in order to enforce a federal law that the FDA itself could not enforce,

A legally permissible approach would be for the MOU to instruct the state agency to determine what level of compounding would constitute inordinate amounts. The state agency could then make its own determination of the most appropriate level for compounding, under existing state pharmacy laws regulating manufacturing, compounding, and distributing of drug products. Such an approach would be consistent with the APA, FDAMA and the long-standing authority of state agencies to regulate the practice of pharmacy.

---

[1] In Wisconsin, the pharmacy statute defines "unprofessional conduct" to include violating any "federal . . . statute or rule which substantially relates to the practice of pharmacy." Wis. Stat. § 450.10(1)(a)2.

111. Conclusion

For the forgoing reasons, we object to the Draft MOU as currently written and we strongly urge FDA to redraft the MOU. The MOU should make clear that state agencies should determine whether a pharmacy is distributing "inordinate amounts" interstate based on the scope and safety of that pharmacy's compounding practices, not on an arbitrary percentage-based numeric limit. Even assuming for the sake of argument that FDA has the authority to define "inordinate amount," it must do so through notice and comment rulemaking as required under the APA, not through a memorandum of understanding with the states.

If implemented, the Draft MOU'S definition of "inordinate amounts" will result in a significant narrowing of treatment options for Madison Pharmacy Associates' patients and for patients of other pharmacies that specialize in compounding products for individual patients based on the prescription of a physician. Such a result conflicts with FDAMA and was not intended by Congress.

Sincerely yours,

Dorothy J. Clarke

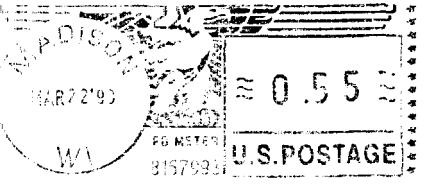
MADISON\40226DJC: DJC

cc Donna Shalala, Secretary of the Department of Health and Human Services
Senator Herbert Kohl
Senator Russell Feingold
Representative Tammy Baldwin
National Association of Boards of Pharmacy
Wisconsin Board of Pharmacy

REINHART | BOERNER | VAN DEUREN
NORRIS & RIESELBACH, S.C.

ATTORNEYS AT LAW

22 East Mifflin Street Suite 600
P. O. Box 2020 Madison, Wisconsin 53701-2020



Ms. Donna Shalala
Secretary of Health and Human Services
200 Independence Avenue, S. W., Room615F
Washington, DC 20201

ROUTING SLIP
GENERATED BY: HP-40
DATE: APR 02, 1999

FDA CONTROL NUMBER: 992195 TRACER #: OS #: 0329990023

DATE OF CORRESPONDENCE: 03/19/99 DATE INTO FDA: 04/02/99

TO: FDA, DOCKETS MANAGEMENT BRANCH (HFA-305)

FROM: DOROTHY J CLARKE, REINHART, BOERNER, VAN DEUREN, NORRIS &RIESELBACH

SYNOPSIS: COPY OF LETTER TO FDA REGARDING DRAFT FEDERAL/STATE MEMORANDUM OF UNDERSTANDING ON INTERSTATE DISTRIBUTION OF COMPOUNDED DRUG PRODUCTS (CC'D SECRETARY SHALALA)

LEAD OFFICE: HFA-305 HOME OFFICE: HF-40

CONTACT/PHONE#: VALERIE A JACKSON WATSON 301-827-4434

COPIES: HFD-1
HF-40 RONALD C VARSACI

COORDINATION:

SIGNATURE REQUIRED:

REFERRALS FROM **HF-40**

ASSIGNED TO	ACTION	DUE DATE
HFA-305	FOR YOUR INFORMATION	

DEPARTMENT OF HEALTH AND HUMAN SERVICES
OFFICE OF THE SECRETARY
EXECUTIVE SECRETARIAT

SECRETARY'S CORRESPONDENCE

OS#: 03/29/1999 0023

From. CLARK, DOROTHY J.

DOL 03/19/1999

On Behalf Of:

Code: Correspondence

Type: General Public

Dt Inc Rec'd: 03/29/1999

Org: REINHART BOERNER VAN DEUREN NORRIS & RIESELBACH/ES:

Add: MADISON, WI

Subject: COPY OF LTR TO FDA REGARDING DRAFT FEDERAL/STATE MEMORANDUM OF UNDERSTANDING ON INTERSTATE DISTRIBUTION OF COMPOUNDED DRUG PRODUCTS

On: 03/29/1999

Assigned to: FDA

ES Dep: White

PC: Friebert

Action: Info. Only

Info Copies: CCC

Interim (Y/N): OS/ES:

Interim Signed:

Final Signed: 03/29/1999

Reply Rec'd in

OPDIV/STAFFDIV ROUTING SECTION
(Recipient should sign & date when received)

sENT TO	DATE	TIME	RECEIVED BY	DATE	TIME

Comment:

99-2195

File Index: PO-4-5

Scheduling ID:

CCC: EVG